AMENDMENT

IN THE CLAIMS:

Please amend claim 2 as indicated in the following list of claims:

1. (Original) A method of identifying a coded test unit in a plurality of coded test units comprising the step of:

contacting the coded test unit with a decoding oligonucleotide comprising an orthogonal nucleobase under conditions in which the decoding oligonucleotide produces a detectable hybridization signal sufficient to distinguish the coded test unit from the remainder of the plurality of coded test units.

2. (Currently Amended) A method for decoding a plurality of coded test units comprising the steps of:

a. identifying a first molecule in the plurality of coded test units according to the method of Claim 1; and

b. identifying a second ~~substrate~~ molecule in the plurality of coded test units according to the method of Claim 1.

3. (Original) The method of Claim 1 wherein the coded test unit is coded with a decoding oligonucleotide comprising an orthogonal nucleobase.

4. (Original) The method of Claim 1 wherein the plurality of coded test units are coded with decoding oligonucleotides, wherein each decoding oligonucleotide independently comprises an orthogonal nucleobase.

5. (Original) The method of Claim 1, 2, 3 or 4 wherein the orthogonal nucleobase is iso-C, iso-G, K, X or H.

6. (Original) The method of Claim 1 wherein the coded test unit comprises a solid substrate.

7. (Original) A method for decoding a plurality of coded substrates comprising the steps of:

a. identifying a first substrate in the plurality of coded substrates according to the method of Claim 6; and

b. identifying a second substrate in the plurality of coded substrates according to the method of Claim 6.

8. (Original) The method of Claim 6 wherein each coded substrate comprises a test moiety.

9. (Original) The method of Claim 8 wherein the test moiety is an oligonucleotide.

10. (Original) The method of Claim 9 wherein a single polynucleotide comprises the test moiety and the coding oligonucleotide.

11. (Original) The method of Claim 9 wherein a first polynucleotide comprises the test moiety and a second polynucleotide comprises the coding oligonucleotide.

12. (Original) The method of Claim 6 wherein the plurality of coded substrates is in an array.

REMARKS

Claims 1-12 are pending and under consideration.

I. AMENDMENT TO THE CLAIMS

Claim 2 has been amended to correct an inadvertent error. Applicant submits that the amendment is fully supported by the specification and claims as originally filed and does not add new matter. Entry of the amendment is kindly requested.

II. REJECTION OF CLAIMS 1-5 UNDER 35 U.S.C. § 102(b)

Claims 1-5 stand rejected under 35 U.S.C. § 102(b), allegedly as being anticipated by Benner (U.S. Patent No. 5,432,272). The Patent Office alleges that Benner teaches the methods recited in claims 1-5. Applicant respectfully traverses the rejection of claims 1-5, since Benner does not teach each and every limitation of any one of claims 1-5.

For a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference. *See In re Bond*, 15 U.S.P.Q.2d 1566, 1567 (Fed. Cir. 1990).

On pages 2-3 of the Office Action dated April 25, 2003, the Patent Office alleges that the subject matter of claim 1 is taught at column 2, line 61, to column 3, line 35, and in Example 2 of Benner (U.S. Patent No. 5,432,272). The Patent Office also alleges that the subject matter of claim 2 is taught at Example 2 and Figure 5 of Benner. The Patent Office specifically points to column 3, lines 6-35, as teaching a method, wherein the coded test unit is coded with a decoding oligonucleotide independently comprising an orthogonal nucleobase selected from iso-C, iso-G, K, X, or H.

With all due respect, Applicant cannot agree with the Patent Office's assessment as to what Benner teaches in the cited sections. Claim 1 of the instant invention recites a method of identifying a coded test unit in a plurality of coded test units comprising contacting the coded test unit with a decoding oligonucleotide comprising an orthogonal nucleobase under conditions in which the decoding oligonucleotide produces a detectable hybridization signal sufficient to distinguish the coded test unit from the remainder of the plurality of coded test units. In contrast, Benner, from column 2, line 61, to column 3, line 35, merely teaches standard, non-standard and orthogonal nucleotide bases, termed by Benner as natural, standard and non-standard bases, respectively, that may fit into a DNA ladder in a standard Watson-Crick duplex in order to increase the "genetic alphabet" from four bases up to twelve bases. Benner identifies the orthogonal base pairing of iso-C with iso-G, K with X, H with J,

and M with N. *See* col. 3, lines 28-35. Benner states that in an enzyme-catalyzed polymerization, it might be possible for each non-standard pyrimidine to recognize uniquely its complementary purine with high fidelity. *See* col. 3, lines 25-28. Example 2 of Benner teaches two chemically synthesized DNA templates (shown in Figure 5 of Benner) containing the base isoC that are suitable for enzyme-based *de novo* DNA strand synthesis where the base isoG must be included in the reaction to generate a full length product. Nowhere from column 2, line 61, to column 3, line 35, Example 2, or anywhere else in Benner, does Benner teach contacting a coded test unit with a decoding oligonucleotide, for example, or teach doing so in a plurality of coded test units, as another example.

Figure 5 of Benner teaches two specific sequences each containing iso-C that can be used as a template for T7 RNA polymerase or else for DNA polymerase. Nowhere in Figure 5, or in Figure 5 in combination with the rest of Benner, does Benner teach contacting a coded test unit with a decoding oligonucleotide, for example, or teach doing so in a plurality of coded test units, as another example.

Benner, at column 3, lines 6-35, teaches the orthogonal bases of iso-C, iso-G, K, X and H. Nowhere in column 3, lines 6-35, or in combination with the rest of Benner, does Benner teach contacting a coded test unit with a decoding oligonucleotide, for example, or teach doing so in a plurality of coded test units, as another example.

Since Benner does not teach contacting a coded test unit with a decoding oligonucleotide, for example, or teach doing so in a plurality of coded test units, as another example, consequently Benner does not teach each and every limitation of claim 1.

Amended claim 2 recites a method for decoding a plurality of coded test units comprising identifying a first molecule according to the method of claim 1 and identifying a second molecule in the plurality according to the method of claim 1. Not only does Benner not teach each and every element of claim 1, as discussed above, but Benner does not teach the step of identifying a second molecule in a plurality of coded test units, as in claim 2 of the instant invention. As explained above, Example 2 of Benner teaches two chemically synthesized DNA templates (shown in Figure 5 of Benner) containing the base isoC that are suitable for enzyme-based *de novo* DNA strand synthesis where the base isoG must be included in the reaction to generate a full length product. Since Benner teaches merely the polymerization of oligonucleotides with orthogonal bases, there simply is no teaching in Example 2 of Benner, in conjunction with Figure 5, or anything else in Benner, that suggests a method of decoding a first and second molecules out of a plurality of coded test units with decoding oligonucleotides, Benner does not teach each and every limitation of claim 2.

Claims 3-5 depend from claim 1, and hence, Benner does not teach each and every limitation of any one of claims 3-5, because, as explained above, Benner does not teach each and every element of claim 1. It makes no difference that Benner teaches, in column 3, lines 6-35, the orthogonal bases of iso-C, iso-G, K, X and H that are also recited in claim 5, since Benner does not teach or even suggest the methods in the claims that claim 5 is dependent upon.

For the foregoing reasons, Applicant respectfully submits that Benner does not teach or suggest each and every limitation recited in any one of methods of claims 1-5 in the instant application. Accordingly, Applicant kindly requests the withdrawal of the rejection of claims 1-5 under 35 U.S.C. § 102(b).

II. REJECTION OF CLAIMS 6-12 UNDER 35 U.S.C. § 103(a)

Claims 6-12 stand rejected under 35 U.S.C. § 103(a), allegedly as being obvious over Benner (U.S. Patent No. 5,432,272) in view of Southern (U.S. Patent 6,054,270). The Patent Office contends that it would have been *prima facie* obvious to one of ordinary skill at the time the invention was made to substitute and combine a method of making an array of oligonucleotides on a solid support, as in Southern, with the "orthogonal nucleobase hybridization method" alleged to be taught by Benner. Applicant respectfully traverses the rejection of claims 6-12 under 35 U.S.C. § 103(a).

The legal standard of *prima facie* obviousness requires that three criteria be met: (1) the prior art, either alone or combination, must teach or suggest each and every limitation; (2) a suggestion or motivation in the cited references or in the art to modify or combine the cited references; and (3) the cited references must provide a reasonable expectation of successfully achieving the claimed invention. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); *In re* Wilson, 165 U.S.P.Q. 494, 496 (CCPA 1970). Applicants respectfully submit that *prima facie* obviousness has not established since these criteria are not met.

Claim 6 recites the method of claim 1 wherein the coded test unit comprises a solid substrate. Claims 7-12 depend from claim 6. The Patent Office contends that Benner teaches the method of claim 1. The Patent Office acknowledges that Benner does not teach a method wherein the coded test unit comprises a solid substrate.

Applicant respectfully submits that Benner (U.S. Patent No. 5,432,272) and Southern (U.S. Patent 6,054,270), either alone or in combination do not teach or suggest each and every limitation of claims 6-12. As explained in Section II above, Benner (U.S. Patent No. 5,432,272) does not teach a method of identifying a coded test unit in a plurality of units

where the decoding oligonucleotide produces a detectable hybridization signal sufficient to distinguish the coded test unit from the remainder of coded test units, as in claim 1 of the instant application. As previously discussed in Section II, Benner teaches orthogonal nucleotide bases, *i.e.*, iso-C, iso-G, K, X, H, J, M, and N, for inclusion into oligonucleotides using enzyme-dependent polymerization. Since Benner merely teaches orthogonal bases and methods involving the incubation of an oligonucleotide template containing one or more of such bases with a polymerase, Benner does not teach or suggest each and every limitation recited in any one of methods of claim 1, claim 6, or any of claims 7-12 that depend from claim 6.

Southern (U.S. Patent 6,054,270) does not teach or suggest any of the elements missing in Benner. Southern teaches a method of making an array of oligonucleotides on a support. Southern does not teach or suggest orthogonal nucleobases, or a method of using a decoding oligonucleotide comprising an orthogonal nucleobase to identify a coded test unit in a plurality of coded test units, as recited in the methods of any of claims 6-12 of the instant application. Therefore, Benner alone, Southern alone, or else both references in combination, cannot teach or suggest each and every limitation in claim 1. Since claims 6-12 depend from claim 1, the combination of Benner and Southern references do not teach or suggest each and every element of claims 6-12. For these reasons, Applicant respectfully requests the withdrawal of the rejection of claims 6-12 under 35 U.S.C. § 103(a).

Applicant further submits that there is no suggestion or motivation in the cited references or in the art to modify or combine the cited references. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 16 U.S.P.Q.2d 1430, 1432 (Fed. Cir. 1990); MPEP § 2143.01.

The Patent Office quotes Southern at column 1, lines 30-33, to explain the motivation to use Southern's method of oligonucleotide arrays on solid support as a "new approach which produces both a fingerprint and a partial or complete sequence in a single analysis . . . without the need for cloning." The Patent Office quotes Benner at column 3, lines 26-28, as stating "it might be possible for each non-standard pyrimidine to recognize uniquely its complementary purine with high fidelity." Applicant submits that each of the quotes taken from Southern and Benner are merely reasons to use the individual methods described by Southern and Benner, respectively; the quoted passages do not suggest or motivate one to modify or combine the cited references. Hence, a suggestion or motivation in the cited references or in the art to modify or combine the cited has not been presented by the Patent

Office, and a case of *prima facie* obviousness has not been made. Accordingly, Applicant respectfully requests the withdrawal of the rejection of claims 6-12 under 35 U.S.C. § 103(a).

CONCLUSION

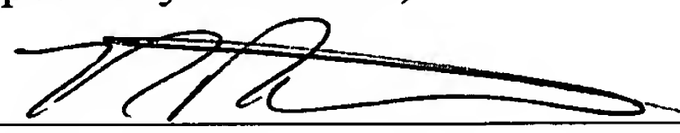
Applicant submits that the claims as presently pending meet all of the criteria for patentability and are in condition for allowance. Early notification to this effect is earnestly solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 849-7607.

No fees are believed due with this response. However, the Commissioner is authorized to charge any fees under 37 C.F.R. § 1.17, any underpayment of fees, or credit any overpayment to Pennie & Edmonds$_{LLP}$ U.S. Deposit Account No. 16-1150 (order no. 9584-030-999) that may be required by this Amendment and Response.

Respectfully submitted,

Date: July 23, 2003



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